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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/717,580	11/21/2003	Frederic Beseme	105045.01	3397

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OLIFF & BERRIDGE, PLC
P.O. BOX 320850
ALEXANDRIA, VA 22320-4850

EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
03/04/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/717,580	BESEME ET AL.	
	Examiner	Art Unit	
	MARIA B. MARVICH	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,41 and 42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 41 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/446,024.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 2, 5, 6, 10, 20-23, 30, 36, 39 and 40 are pending in this application. This office action is in response to an amendment filed 11/10/08.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 2, 41 and 42 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or and substantial asserted utility or a well-established utility.

Claim 1 is drawn to a retroviral RNA molecule in isolated or purified state that is obtainable from tissue, comprising the RNA complement of SEQ ID NO:11. SEQ ID NO:11 is a DNA isolated from human tissue that applicants propose is a member of human endogenous retroviruses. Claim 2 is drawn to an RNA molecule in isolated or purified state, that is obtainable from tissue, comprising a nucleotide sequence comprising the RNA complement of a functional part of SEQ ID NO:11 that encodes at least one *env* retroviral protein such as SEQ IDNO:33-35. Finally, claim 42 is drawn to a probe or primer consisting of a sequence selected from the group consisting of SEQ ID NO:s 16-28. Applicants have screened a cDNA library using a Ppol-MSRV probe (SEQ ID NO:29) and detected overlapping clones thus arriving at a reconstructed putative genomic RNA from smaller clones detected, SEQ IDNO:11. The reconstructed RNA sequence is deduced from the alignment of overlapping clones and encodes a series of retroviral like structures, R-U5-gag-pol-env-U3-R, and the sequences are found on

multiple chromosomes (see paragraph 0002). Applicants have called this sequence HERV-W. The reconstructed sequence is integrally contained in clone RG083M05, which comprises two discontinuous regions that are 96% similar to the reconstructed genome. Biologically, applicants teach that HERV-W (1) potential association with pathologies due to its restricted expression in placenta i.e. potential expression from LTRs of operably linked genes (2) potential fusogenic role of the envelope proteins wherein the fetus could be protected from maternal immune systems (3) potential protection by the envelope protein against exogenous retroviral infection (4) impairment of local cellular immunity by a potential immunostimulatory signal carried by the envelope.

SEQ ID NO:11 has been identified by applicants, applicants have determined that this sequence is a member of the HERV-w family of endogenous retroviruses. However, neither the art nor the specification support a utility for SEQ ID NO:11 at the time of filing. As set forth below in greater detail,

For "specific utility", the invention must have a utility specific to the subject matter claimed in contrast with a general utility that would be applicable to the broad class of the invention. According to 35 U.S.C. 101, a specific utility is not a list of potential applications for which the broad class of the invention would also have utility. To be specific, the application must teach the skilled artisan in specific terms specific biological activities of the retroviral RNA molecule, and reasonably correlate that activity to a disease condition. The instant specification is limited to conjecture as to potential disorders that HERV-w might be associated. The specification suggests that the sequence can be a molecular marker for an autoimmune disorder, or a molecular marker for a pathology that is associated with a pathological pregnancy, or a

chromosomal marker for susceptibility to an autoimmune disease. Further, applicants disclose that a nucleotide fragment would be useful as a diagnostic composition, such as in diagnostic hybridization techniques (see paragraph 0078). Specifically, the specification discloses that the HERV-W is expressed in placenta, but merely speculates about the function in placenta and suggest that expression of the HERV-W in the placenta may be under the control of isolated LTR and may result in pathology from aberrant expression. Applicants speculate on a fusogenic role at the level of cellular subtypes in the placenta, an immunosuppressive role and a protective role (see paragraph 0008-0010). There is no description of how the structure of the putative genomic RNA sequence identified as SEQ ID NO:11 relates to the proposed functions. Beyond expression in the placenta, and identity to genes potentially encoding retroviral env, pol and gag sequences, the specification has not described characteristics or specific regions of SEQ ID NO:11 that would provide a correlation between structure and function. It is not clear, whether HERV-W expression is detectable or where HERV-W elements are expressed or if wild-type HERV-w is to be associated with the disorder or if there are unidentified mutant versions of HERV-w that can be associated with disease. Most specifically, it is noted that HERV-w is a family of retroviral elements. Nonetheless such ability to distinguish between pathological states and normal, healthy states would require an identification of what distinctions exists in HERV-w in each state. None such criteria or direction or guidance is provided in the art or specification. Even should a function for the family be demonstrated, it is not clear that SEQ ID NO:11 will share that function. Hence, applicants do not provide a specific utility for HERV-W.

"Substantial utility" defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are

not substantial utilities. The instant claims propose functions for HERV-W that would require basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved. The substantial use of HERV-W must be assessed at the time of filing. At that time, the molecular, physiological and biochemical characterization of HERV-W was lacking. Song-An et al teach in post filing art (2001) the first HERV-w *env* gene demonstrated to encode the functional properties of a retrovirus envelope glycoprotein (see abstract). However, HERV-w env is expressed from HIV but is not expressed from the HERV-W sequence. It is not clear that HERV-w elements are expressible at this date. As well, Song-An teach that whether HERVs can assemble into infectious virions even with transcomplementation with virion proteins from other HERVs is unknown (see page 3488, col 2, ¶2). Hence, here several years post-filing, the art teaches that HERV-w is difficult to characterize. In 2007, data was presented that suggested that HERV-W elements might be expressed but still to date whether the elements or HERV-W are potential causative agents of various disease was still required. And in 2008, the link between HERV and disease is no closer to being known as Dolei et al teach that At present, it is unclear whether the detection of MSRV/HERV-W/syncytin expression simply represents an epiphenomenon (e.g., the abnormal expression of endogenous HERV-W or an unrelated coinfection) or whether it might play some part in pathogenesis (Dolei, 2006; Perron and Seigneurin, 1999). In a domain where many questions still remain unanswered, there is experimental evidence linking the presence and regulation of MSRV (the first HERV-W element detected and purified as retroviral particles carrying RT and the corresponding HERV-W RNA, in LTR, gag, pol, and env regions) with MS features. Indeed, we are only beginning to

understand a yet poorly explored domain in human biology, that of endogenous retroviruses." Again this does not indicate whether SEQ ID NO:11 shares these potential correlations as unraveling the role of a family member does not ensure that all members will perform the same function. Hence, it is clear that applying the instant asserted utilities to a real-world problem requires that some specific useful feature of the nucleic acid molecule is known.

Finally, the invention lacks "well-established utility" in that the disclosure provides no specific teaching of the functional properties of the claimed nucleic acid or its encoded protein. While the specification asserts that the claimed sequence has potential role in the development of autoimmune disease such as multiple sclerosis and rheumatoid arthritis, in unsuccessful pregnancy or pathological conditions of pregnancy, there is a lack of evidence presented to indicate any association of the sequence to such pathologies. In 2000, Gaudin et al teach that despite proposals that based upon HIV and HTLVs correlations with rheumatoid arthritis, HERV-w shows no such association. Hence, applicants' assertions lack well established utility. Furthermore, while applicants' claim an RNA molecule comprising a nucleotide sequence comprising the complement of at least an envelope protein, applicants mean SEQ IDNO:33-35. However, applicants have not demonstrated that these are envelope proteins or that these sequences can be expressed. A review of known HERV-w family envelope protein members demonstrates that none of SEQ ID NO:33-35 share any homology with known proteins (see figure 2, Kim et al). Hence, applicants' claims lack well-established utility. It is noted that if the molecule lacks utility the need or use of probes or primers are equally void of utility.

Claim Rejections - 35 USC § 112

Comment [S1]: see S2

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 41 and 42 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention, and for the additional reasons set forth below.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based on a single factor but is rather a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter, 1986) and In *re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988); these factors include the following:

SEQ ID NO:11 is the DNA complement of RNA that is a member of human endogenous retroviruses. The instant claims are drawn to a retroviral RNA molecule that is the complement of SEQ ID NO:11 and as part of a diagnostic composition. The specification discloses that SEQ ID NO:I 1 is a reconstructed putative genomic RNA from smaller clones detected by screening a cDNA library with Ppol- MSRV probes (see Figure 1). SEQ ID NO:11 encodes a structure of R-U5-gag-pol-env-U3-R, which is found on multiple chromosomes (see paragraph 0002).

Applicants have aligned the reconstructed sequence with the genomic clone and found that it exhibits 96% similarity with two discontinuous regions of genomic clone RG083M05 where it is integrally. From this alignment, the Applicants have deduced an LTR sequence and identified elements characteristic of retroviruses. Applicants have called this sequence HERV-W.

HERV-W is a family of retrovirus of which MSRV was the first member identified. Applicants propose use of SEQ ID NO:11 as a diagnosis of states of pathological pregnancy or of unsuccessful pregnancy and of autoimmune disease such as multiple sclerosis or rheumatoid arthritis. The proposed use of SEQ ID NO:11 have no specific and substantial and well - established utility. For example, while applicants propose use of SEQ IDNO:11 there is no indication to date more then a decade past filing of the application that HERV-w is known to correlate to any diseases. In fact, despite being initially linked to rheumatoid arthritis there is no indication that such a link exists (see Gaudin et al). Yet, the function of SEQ ID NO:11 has not been established therefore this is not a substantial real world utility because it would require additional experimentation to reasonably confirm. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. The instant claims propose a function for the SEQ ID NO:11 that would require basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved. Beyond expression in the placenta, and identity to genes potentially encoding retroviral env, pol and gag sequences, the specification has not described characteristics or specific regions of SEQ ID NO:11 that would provide a correlation between structure and function. It is not clear, whether HERV-W expression is detectable or where HERV-W elements are expressed or if wild-type HERV-w is to be associated with the disorder

or if there are unidentified mutant versions of HERV-w that can be associated with disease. Most specifically, it is noted that HERV-w is a family of retroviral elements. Finally, applicants have neither established a role for HERV-w or SEQ ID NO:11 in disease state nor have applicants' demonstrated that the sequences of SEQ IDNO:11 such as env, gag or pol are actually expressed. It is not clear that SEQ ID NO:11 is anything more then dead genomic DNA. Applying these asserted utilities to a real-world problem requires that some specific useful feature of the nucleic acid molecule is known.

Secondly, it is noted that the claims recite that the RNA molecule is obtainable from tissue. However, evidence only exists that the DN is obtainable from tissue.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARIA B. MARVICH whose telephone number is (571)272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Maria B Marvich, PhD
Primary Examiner
Art Unit 1633

/Maria B Marvich/
Examiner, Art Unit 1633